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EXAMINER	
FORMAN, BETTY J	

ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)
	08/619,649	DRMANAC, RADOJE
	Examiner	Art Unit
	Betty Forman	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *97,157-182 and 184-188* is/are pending in the application.

4a) Of the above claim(s) *176* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *97 157-175 178-182 184-188* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5 May 2011 has been entered.

Status of the Claims

This action is in response to papers filed 5 May 2011 in which claims 181 and 186 were amended and the previous rejections were traversed.

The amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 12 November 2010 are maintained.

Applicant's arguments have been thoroughly reviewed and are discussed below. Additionally, in the interest of expedited prosecution, new grounds for rejection are discussed.

Claims 97, 157-175, 177-182, 184-188 are under prosecution.

Claim Objections

Applicant is advised that should claim 186 be found allowable, claim 182 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 181-182 and 186 are rejected under 35 U.S.C. 102(b) as being anticipated by Stavrianopoulos et al (U.S. Patent No. 4,994,373, issued 19 February 1991).

Regarding Claims 181-182 and 186, Stavrianopoulos teaches an array of wells comprising immobilized analytes (Example 1-7) the wells providing physical barriers between each section of immobilized analytes. Stavrianopoulos teaches either the

probe (Example 6) and/or analyte (Example 7) is immobilized in each well thereby providing at least two different oligonucleotides in each well. Stavrianopoulos further defines the analyte as “admixtures”, “biological systems containing nucleic acids”, DNA, RNA, and single or double-stranded oligonucleotides (Column 1, lines 27-37) thus providing multiple analytes applied to each well. The instant claims define each array having different sequences attached. The combined probe/analyte and admixture of analytes as defined by the reference are encompassed by the claim because they provide at least two different sequences attached to each well either via the fixing described in Example 1 or via the hybridization described in Examples 6-7).

Claims 181-182 and 186 are rejected under 35 U.S.C. 102(e) as being anticipated by Douglas (U.S. Patent No. 5,556,748, filed 30 July 1996).

Regarding Claims 181-182 and 186, Douglas teaches a support comprising an array of wells forming physical barriers between the assay sections (Column 5), each section having salmon sperm DNA, a ligating DNA probe, a labeled DNA probe and a target DNA thereby providing oligonucleotides of different sequences attached to each array section (Fig. 3, Column 10, lines 5-50).

Claims 181-182 and 186 are rejected under 35 U.S.C. 102(e) as being anticipated by Barany et al (U.S. Patent No. 5,494,810, filed 2 November 1992).

Regarding Claims 181-182 and 186, Barany teaches a support comprising an array of wells forming physical barriers between the assay sections (Column 42, lines 6-12 and Fig. 6), each section having ligated and non-ligated DNA probes (Fig. 6) thereby providing oligonucleotides of different sequences attached to each array section.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 181-182 and 184-188 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barany et al (U.S. Patent No. 5,494,810, filed 2 November 1992).

Regarding Claims 181-182 and 184-186, Barany teaches a support comprising an array of wells forming physical barriers between the assay sections (Column 42, lines 6-12 and Fig. 6), each section having ligated and non-ligated DNA probes (Fig. 6) thereby providing oligonucleotides of different sequences attached to each array section.

Barany teaches the ELISA-based device was used to run a number of experiments listing six different biotinylated primers (Table VII). The microtiter plate used in ELISA-based assay has 96 wells. Given the 3 target genes and six biotinylated primers, it would have been obvious to one of ordinary skill the some of the wells had

the same probes and some of the wells had different probes. It was standard procedure at the time of the instant invention to perform duplicate reactions thereby it would have been obvious to provide multiple wells of the microtiter plate with the same probes for the well-known purpose of reaction confirmation. It would have been further obvious to use one plate for of the 3 target genes thereby providing different array sections on the plate. The artisan would have been motivated to perform all the assays simultaneously on a single plate thereby economizing on time.

Claims 97, 157-175, 177-182, 184, 186-187 are rejected under 35 U.S.C. 103(a) as being unpatentable over Southern et al (Genomics, 1992, 13: 1008-1017) in view of Kauvar (U.S. Patent No. 5,356,784, issued 18 October 1994) and/or Wang (U.S. Patent No. 4,618,475, issued 21 October 1986).

Regarding Claims 97, 157-158, 166-168, 177-182 and 186, Southern discloses a support comprising an array of four microchips, each having an array of oligonucleotide probes immobilized thereon (Fig. 3, figure legend, line 1). Southern teaches each array is in one of four quadrants on the surface (Fig. 3). The four-quadrant arrangement is encompassed by the physical separation because a quadrant defines a physical location of the surface. Assignment of an array to a quadrant defines a boundary between quadrants, the boundary being the point of physical separation. The reference specifically teaches that the arrays are physically separated i.e. "[T]o quantify the intensity in each cell, **a grid** was superimposed over the array so that each spot lay

at approximately the center of **the grid**" (emphasis added: lines 8-9 of figure legend for Fig. 3). Thus, the reference specifically teaches a grid delineating the arrays but does not specifically teach the grid provides a physical barrier for keeping the arrays and/or probes in corresponding arrays. However, physical barriers grooved and/or hydrophobic were well known in the hybridization art at the time the invention was made as taught by Kauvar and Wang. Kauvar teaches an array of reaction regions on a solid support, each region having a plurality of ligands immobilized in the region wherein the regions are separated by a hydrophobic barriers (Column 7, lines 39-45) whereby reactions within the regions are defined thereby simplifying interpretation of assay results (Column 4, lines 37-58). Wang also teaches an array of reaction areas separated by hydrophobic barriers whereby cross-contamination is virtually eliminated and an "excellent appearance of the final product" is obtained (Column 4, lines 22-53).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the physical separation of Wang and/or Kauvar to the multiple arrays of Southern based on the grid teaching of Southern. One of ordinary skill in the art would have been motivated to do so, with a reasonable expectation of success, for the expected benefit obtaining clearly defined assay results as is well known and routinely practiced in the art of bio-assays (Kauvar, Column 4, lines 37-58 and Wang, Column 4, lines 22-53).

Regarding Claims 159 and 169, Southern discloses the support wherein the microchips are arranged in multiple rows and columns (i.e. two rows and two columns,

Fig. 3). And Kauvar teaches the arrays in an orderly design pattern" (Column 4, line 60) and Wang teaches the similar support comprising multiple rows (Fig. 1).

Regarding Claims 160 and 170, Southern discloses the support wherein the microchips are positioned for use with a multichannel pipette (Fig. 3). The arrays of Southern are arranged in two rows of two columns. While Southern does not teach use of a multichannel pipette, the courts have stated that a claim containing a "recitation with respect to the manner in which a claimed apparatus is intended to be employed does not differentiate the claimed apparatus from a prior art apparatus" if the prior art apparatus teaches all the structural limitations of the claim. Ex parte Masham, 2 USPQ2d 1647 (Bd. Pat. App. & Inter. 1987). Southern teaches the structural elements of the claim and therefore, teaches the support of Claims 160 and 170.

Regarding Claim 161 and 171, Kauvar teaches the apparatus is used with labeled reagents and wash buffer (Column 5, line 55-Column 6, line 15). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the reagents used with the apparatus into a kit format for the well-known benefits of kit convenience.

Regarding Claims 162 and 172, Southern teaches a 4 by 4 array but does not teach an 8 by 12 array. However, spotting probes in an 8 x 12 format (i.e. microtiter plate) was well known and routinely practiced in the art at the time the invention was made as taught by Kauvar who further teaches that any convenient or orderly pattern are chosen based on convenience (Column 4, lines 58-64).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the 8 by 12 format of Kauvar to the arrays of Southern based on desired format as taught by Kauvar (Column 4, lines 58-64).

Regarding Claims 163 and 173, Southern discloses the support wherein the array of microchips comprises more than 256 probes i.e. each of the four microchips has 256 probes. Hence, the support of Claim 97 has more than 256 probes per array as claimed.

Regarding Claims 164 and 174, Southern discloses the support wherein the probes are between 4 and 9 bases (Fig. 3).

Regarding Claims 165 and 175, Southern discloses the support wherein the probes are synthesized on the support (page 1009, left column). Southern does not teach light-directed synthesis. However, the courts have stated that "even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) see MPEP 2113. Because determination of patentability is based on the product and because Southern teaches the product, the process of making the product as recited in the claim does not define the product over that of Southern.

Regarding Claims 184 and 187, Southern teaches the support has duplicate arrays thereby providing arrays that are identical to other arrays, but different from others (Fig. 4 and accompanying text).

4. Claims 97, 157-175, 177-189 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drmanac et al (Electrophoresis, 1992, 13:566-573) in view of Kauvar (U.S. Patent No. 5,356,784, issued 18 October 1994) and/or Wang (U.S. Patent No. 4,618,475, issued 21 October 1986).

Regarding Claims 97, 157-158, 166-168, 177-182 and 186 Drmanac discloses a support comprising multiple microarrays (Fig. 4), each comprising an array of differing oligonucleotides immobilized thereon wherein the microarrays are separated from each other. The arrays illustrated in Fig. 4 clearly appear to be separated by a barrier, and the reference teaches that hybridization with different samples requires separation (page 571, last paragraph). The reference does not specifically teach physical barriers for keeping the arrays and/or probes in corresponding arrays. However, physical barriers grooved and/or hydrophobic were well known in the hybridization art at the time the invention was made as taught by Kauvar and Wang.

Kauvar teaches an array of reaction regions on a solid support, each region having a plurality of ligands immobilized in the region wherein the regions are separated by a hydrophobic barriers (Column 7, lines 39-45) whereby reactions within the regions are defined thereby simplifying interpretation of assay results (Column 4, lines 37-58).

Wang also teaches an array of reaction areas separated by hydrophobic barriers whereby cross-contamination is virtually eliminated and an "excellent appearance of the final product" is obtained (Column 4, lines 22-53).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the physical separation of Wang and/or Kauvar to the multiple arrays of Drmanac. One of ordinary skill in the art would have been motivated to do so, with a reasonable expectation of success, for the expected benefit obtaining clearly defined assay results as is well known and routinely practiced in the art of bio-assays (Kauvar, Column 4, lines 37-58 and Wang, Column 4, lines 22-53).

Regarding Claims 159 and 169, Drmanac teaches the support wherein the microchips are arranged in multiple rows and columns (Fig. 4). And Kauvar teaches the arrays in an orderly design pattern" (Column 4, line 60) and Wang teaches the similar support comprising multiple rows (Fig. 1).

Regarding Claims 160,170, 183 and 189 Drmanac teaches the support wherein the microchips are "positioned" for use with a multichannel pipette (i.e. arrayed, Fig. 4).

Regarding Claim 161 and 171, Drmanac teaches hybridization reagents (page 571). Hardy teaches the similar support and hybridization reagents (Column 11).

Regarding Claims 162 and 172, Drmanac teaches the arrays are arrayed in 8 by 12 format (paragraph spanning pages 569-570).

Regarding Claims 163 and 173, Drmanac teaches the support wherein the array of microchips comprises more than 256 probes (page 569-570).

Regarding Claims 164 and 174, Drmanac teaches the support wherein the probes of between 4 and 9 bases are spotted onto the arrays for hybridization (page 571).

Regarding Claims 165 and 175, Drmanac teaches the support of Claims 97 and 166 as discussed above. While the reference does not teach light-directed synthesis. However, the courts have stated that "even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) see MPEP 2113. Because determination of patentability is based on the product and because the combination of Drmanac and Hardy teach the product, the process of making the product as recited in the claim does not define the product over the prior art.

Regarding Claims 184-185 and 187-188, Drmanac teaches the support has duplicate arrays thereby providing arrays that are identical to other arrays, but different from others (Fig. 4 and accompanying text).

Response to Arguments

5. Applicant asserts that the instantly claimed device differs from the cited prior art in that the present invention is used to identify different analytes. Applicant argues that

the arrays of Southern only permit replica measurement of the same reaction but does not permit use of different probes for different hybridization reactions.

The asserted utility is noted. However, the claims are not limited by the intended use as asserted. The instant claims merely define arrays of oligonucleotide probes having different sequences and separated by physical barriers. It is maintained that Southern teaches a device very similar to that claimed. The reference only differs in the physical barrier between the arrays. However, the reference teaches a "grid" overlaying the support which clearly suggests the barrier as claimed.

Applicant further argues that Southern's arrangement of four arrays provides parallel use of the arrays in the same hybridization reaction but not different probes for use in individual arrays. Applicant argues that one of ordinary skill would not be motivated to combine the teaching of Southern and Kauvar because the references are interested in different endeavors i.e. Southern is interested in sequencing and Kauvar is interested in analyte detection.

The argument has been considered but is not found persuasive because both Southern and Kauvar are interested in detecting region-specific signals. Southern specifically teaches “[T]o quantify the intensity in each cell, a grid was superimposed over the array so that each spot lay at approximately the center of the grid” (lines 8-9 of figure legend for Fig. 3). Kauvar is also interested in region-specific signal detection "convenience and simplicity of interpreting results” (Column 4, lines 53-55). Hence, Southern and Kauvar have a common goal of detecting region-specific signals. It is maintained that the combination of Southern and Kauvar is reasonable and that adding

the barriers of Kauvar to the arrays of Southern would have been an obvious modification at the time of the instant invention.

Applicant argues that the combination of Southern and Wang does not render the invention obvious because Wang does not teach why it would be desirable or necessary to place their hydrophobic material between the four arrays of Southern. Applicant asserts that absent a teaching in Southern or Wang that modification of Southern would be required, the skilled artisan would not have been motivated to do so.

In response to applicant's argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and KSR International Co. v. Teleflex, Inc., 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, as stated in the rejection, Wang clearly teaches the advantages of providing barriers to separate assay regions. It is maintained that it would have been obvious to apply the separating barriers of Wang to the substrate of Southern to prevent cross-contamination between assay regions and obtain assay region-specific detection as desired by Southern as evidenced by the use of a grid overlay.

Furthermore, given the multiple arrays of Southern it would have obvious to one of ordinary skill to apply the barriers of Kauvar and/or Wang to thereby extend the

usefulness of Southern's multiple arrays. Based on the teaching of Kauvar and/or Wang the artisan would have recognized that adding barriers to Southern's arrays would have allowed differential assays along with Southern's desired differential detection thereby extending the usefulness of the multiple arrays. It is maintained that the combination of Southern and Kauvar and/or Wang is reasonable and that adding the prior art barriers to the arrays of Southern would have been obvious to one of ordinary skill at the time of the instant invention.

Regarding the rejection over Drmanac in view of Kauvar and Wang, Applicant argues that Drmanac does not immobilize the probes and therefore separation of the different areas is not critical and because separation is not critical, there would be no reason to provide the areas with the barriers of Kauvar and/or Wang. Applicant further argues that one of ordinary skill would not be motivated to combine the teaching of Drmanac and Kauvar and/or Wang because the references are interested in different endeavors i.e. Drmanac is interested in target identification and Kauvar is interested in increased sensitivity of analyte detection.

The argument has been considered but is not found persuasive because all of Drmanac, Kauvar and Wang are all interested in detecting region-specific signals based on analyte binding. Hence, Southern, Kauvar and Wang have a common goal of detecting region-specific signals. Furthermore, it would have obvious to one of ordinary skill to apply the barriers of Kauvar and/or Wang to the multiple arrays of Drmanac thereby extend the usefulness of Drmanac's multiple arrays. Based on the teaching of Kauvar and/or Wang the artisan would have recognized that adding barriers to

Drmanac's arrays would have allowed differential assays in addition to region-specific detection thereby extending the usefulness of the multiple arrays. It is maintained that the combination of Drmanac and Kauvar and/or Wang is reasonable and that adding the barriers of Kauvar and/or Wang to the arrays of Drmanac would have been an obvious modification at the time of the instant invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Betty Forman whose telephone number is (571)272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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